SEQUENCE LISTING

:110> Bayerische Julius-Maximilians-Universität Würzburg

:120> Mutein of a bone morphogenetic protein and use thereof

<130> S 10019 PCT

<160> 33

<170> PatentIn version 3.1

<210> 1

<211> 114

<212> PRT

<213> Homo sapiens

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<223> BMP-2

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His Pro Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn Asp Trp Ile 20 25 30

Val Ala Pro Pro Gly Tyr His Ala Phe Tyr Cys His Gly Glu Cys Pro 35 40 45

Phe Pro Leu Ala Asp His Leu Asn Ser Thr Asn His Ala Ile Val Gln 50 55

Thr Leu Val Asn Ser Val Asn Ser Lys Ile Pro Lys Ala Cys Cys Val 65 70 75 80

Pro Thr Glu Leu Ser Ala Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu 85 90 95

Lys Val Val Leu Lys Asn Tyr Gln Asp Met Val Val Glu Gly Cys Gly
100 105 110

Cys Arg

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<210> 3 <211> 116 <212> PRT <213> Homo sapiens

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<400> 3

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Arg Arg His Ser Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn Asp 20

Trp Ile Val Ala Pro Pro Gly Tyr Gln Ala Phe Tyr Cys His Gly Asp 35 40

Cys Pro Phe Pro Leu Ala Asp His Leu Asn Ser Thr Asn His Ala Ile 50 55 60

Val Gln Thr Leu Val Asn Ser Val Asn Ser Ser Ile Pro Lys Ala Cys 65 70 75 80

Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu Tyr Leu Asp Glu 85 90

Tyr Asp Lys Val Val Leu Lys Asn Tyr Gln Glu Met Val Val Glu Gly 100 105 110

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															gcctgt	
															aaggtg	
grai	ctga	laaa	acta	ccag	ga g	atgg	ragt	a ga	.ggga	tgtg	ggt	gccg	ctg	a		
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Lys	His	Glu 35	Leu	Tyr	Val	Ser	Phe 40	Arg	Asp	Leu	Gly	Trp 45	Gln	Asp	Trp	
Ile	Ile 50	Ala	Pro	Glu	Gly	Tyr 55	Ala	Ala	Phe	Tyr	Cys 60	Asp	Gly	Glu	Cys	
Ser 65	Phe	Pro	Leu	Asn	Ala 70	His	Met	Asn	Ala	Thr 75	Asn	His	Ala	Ile	Val 80	
Gln	Thr	Leu	Val	His 85	Leu	Met	Phe	Pro	Asp 90	His	Val	Pro	Lys	Pro 95	Cys	

Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp 100 105 110

Ser Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ser 115 120 125

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<223> BMP-5

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Ser Ser Ala Ser Asp Tyr Asn Ser Ser Glu Leu Lys Thr Ala Cys Arg 20 25 30

Lys His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Gln Asp Trp 35 40 45

Ile Ile Ala Pro Lys Gly Tyr Ala Ala Asn Tyr Cys Asp Gly Glu Cys 50 60

Ser Phe Pro Leu Asn Ala His Met Asn Ala Thr Asn His Ala Ile Val 65 70 75 80

Gln Thr Leu Val His Leu Met Asn Pro Glu Tyr Val Pro Lys Pro Cys 85 90 95

Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp 100 105 110

Asn Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala 115 120 125

Cys Gly Cys His

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<212> DNA

<213> Homo sapiens

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<223> BMP-6

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<211> 139

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<222> (1)..(139)

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Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu Asn Ser Ser Ser 20 25 30

Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr Val Ser Phe Arg 35

Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala Ala 50 55 60

Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Leu Asn Ser Tyr Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His Phe Ile Asn Pro 85 90 95

Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln Leu Asn Ala Ile 100 105 110

Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile Leu Lys Lys Tyr 115 120 125

Arg Asn Met Val Val Arg Ala Cys Gly Cys His
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<210> 10

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<212> DNA

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cacgagctgt atgtcagctt ccgagacctg ggctggcagg actggatcat cgcgcctgaa 180
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aagccctgct gtgcgcccac gcagctcaat gccatctccg tcctctactt cgatgacagc 360
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<211> 139

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Pro Gln Ala Asn Arg Leu Pro Gly Ile Phe Asp Asp Val His Gly Ser 20 25 30

His Gly Arg Gln Val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln 35 40 45

Asp Leu Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala 50 55 60

Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Leu Asp Ser Cys Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro 85 90 95

Asn Ala Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr 100 105 110

Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His 115 120 125

Arg Asn Met Val Val Lys Ala Cys Gly Cys His
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<211> 120

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<223> GDF-5

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Ala Arg Cys Ser Arg Lys Ala Leu His Val Asn Phe Lys Asp Met Gly 20 25 30

Trp Asp Asp Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Phe His Cys 35

Glu Gly Leu Cys Glu Phe Pro Leu Arg Ser His Leu Glu Pro Thr Asn 50 55 60

His Ala Val Ile Gln Thr Leu Met Asn Ser Met Asp Pro Glu Ser Thr 65 70 75 80

Pro Pro Thr Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser Ile Leu 85 90 95

Phe Ile Asp Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met 100 105 110

Val Val Glu Ser Cys Gly Cys Arg 115 120

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363

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105

110

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60

120

180

240

300

360

Val Val Glu Ser Cys Gly Cys Arg 115 120 16 <210> 360 <211> DNA <212> <213> Mus musculus <220> <221> misc\_feature <222> (1)..(360) <223> GDF-6 <400> 16 accgccttcg ccagccgtca cggcaagcga catggcaaga agtccaggct gcgctgcagc agaaagcctc tgcacgtgaa ttttaaggag ttaggctggg acgactggat tatcgcgccc ctagagtacg aggcctatca ctgcgagggc gtgtgcgact ttccgctgcg ctcgcacctt gagcccacta accatgccat cattcagacg ctgatgaact ccatggaccc gggctccacc ccgcctagct gctgcgttcc caccaaactg actcccatta gcatcctgta catcgacgcg ggcaataatg tagtctacaa gcagtatgag gacatggtgg tggagtcctg cggctgtagg <210> 17 146 <211> <212> PRT <213> Mus musculus <220> MISC FEATURE <221> <222> (1)...(146)<223> GDF-7<400> 17 Thr Ala Leu Ala Gly Thr Arg Gly Ala Gln Gly Ser Gly Gly Gly 10 15 20 25 30 Ala Gly Arg Gly His Gly Arg Arg Gly Arg Ser Arg Cys Ser Arg Lys 35 40 45 Ser Leu His Val Asp Phe Lys Glu Leu Gly Trp Asp Asp Trp Ile Ile 50 55 60

Ala Pro Leu Asp Tyr Glu Ala Tyr His Cys Glu Gly Val Cys Asp Phe 70 75 80

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Pro Leu Arg Ser His Leu Glu Pro Thr Asn His Ala Ile Ile Gln Thr 85 90 95

Leu Leu Asn Ser Met Ala Pro Asp Ala Ala Pro Ala Ser Cys Cys Val 100 105 110

Pro Ala Arg Leu Ser Pro Ile Ser Ile Leu Tyr Ile Asp Ala Ala Asn 115 120 125

Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu Ala Cys Gly 130 135 140

Cys Arg

145

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Lys Glu Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Pro Gly Tyr Glu 20 25 30

Ala Tyr Glu Cys Arg Gly Val Cys Asn Tyr Pro Leu Ala Glu His Leu
35 40 45

Thr Pro Thr Lys His Ala Ile Ile Gln Ala Leu Val His Leu Lys Asn 50 60

Ser Gln Lys Ala Ser Lys Ala Cys Cys Val Pro Thr Lys Leu Glu Pro 65 70 75 80

Ile Ser Ile Leu Tyr Leu Asp Lys Gly Val Val Thr Tyr Lys Phe Lys 90 95

Tyr Glu Gly Met Ala Val Ser Glu Cys Gly Cys Arg 100 105

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aactacecee tggcagagea teteacacee acaaageatg caattateea ggeettggte 180
caceteaaga atteecagaa agetteeaaa geetgetgtg tgeccacaaa getagageee 240
ateteeatee tetatttaga caaaggegte gteacetaca agtttaaata egaaggeatg 300
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<210> 21

<211> 110

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<222> (1)..(110)

<223> GDF-2

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Phe Glu Asp Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Lys Glu Tyr 20 25 30

Glu Ala Tyr Glu Cys Lys Gly Gly Cys Phe Phe Pro Leu Ala Asp Asp 35 40 45

Val Thr Pro Thr Lys His Ala Ile Val Gln Thr Leu Val His Leu Lys 50 55

Phe Pro Thr Lys Val Gly Lys Ala Cys Cys Val Pro Thr Lys Leu Ser 70 75 80

Pro Ile Ser Val Leu Tyr Lys Asp Asp Met Gly Val Pro Thr Leu Lys 85 90 95

Tyr His Tyr Glu Gly Met Ser Val Ala Glu Cys Gly Cys Arg
100 105 110

<210> 22

<211> 333

<212> DNA

<213> Homo sapiens

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<222> (1)..(333)

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ggetgggaca getggateat tgeaceeaag gagtatgaag eetaegagtg taagggegge 120
tgettettee eettggetga egatgtgaeg eegaegaaac acgetategt geagaeeetg 180
gtgeatetea agtteeeac aaaggtggge aaggeetget gtgtgeeeac eaaactgage 240
eecateteeg teetetaeaa ggatgaeatg ggggtgeeea eecteaagta eeattaegag 300
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<210> 23

<211> 114

<212> PRT

<213> Homo sapiens

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His Pro Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn Asp Trp Ile 20 25 30

Val Ala Pro Pro Gly Tyr His Ala Phe Tyr Cys His Gly Glu Cys Pro 35 40 45

Phe Pro Pro Ala Asp His Leu Asn Ser Thr Asn His Ala Ile Val Gln 50 60

Thr Leu Val Asn Ser Val Asn Ser Lys Ile Pro Lys Ala Cys Cys Val 65 70 75 80

Pro Thr Glu Leu Ser Ala Ile Ser Met Leu Tyr Leu Asp Glu Asn Glu 85 90 95

Lys Val Val Leu Lys Asn Tyr Gln Asp Met Val Val Glu Gly Cys Gly
100 105 110

Cys Arg

<210> 24

<211> 116

<212> PRT

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Arg Arg His Ser Leu Tyr Val Asp Phe Ser Asp Val Gly Trp Asn Asp 20 25 30

Trp Ile Val Ala Pro Pro Gly Tyr Gln Ala Phe Tyr Cys His Gly Asp 35 40 45

Cys Pro Phe Pro Pro Ala Asp His Leu Asn Ser Thr Asn His Ala Ile 50 55

Val Gln Thr Leu Val Asn Ser Val Asn Ser Ser Ile Pro Lys Ala Cys 65 70 75 80

Cys Val Pro Thr Glu Leu Ser Ala Ile Ser Met Leu Tyr Leu Asp Glu 85 90 95

Tyr Asp Lys Val Val Leu Lys Asn Tyr Gln Glu Met Val Val Glu Gly
100 105 110

Cys Gly Cys Arg 115

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<211> 132

<212> PRT

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<222> (1)..(132)

<223> BMP-5 mutein

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1 10 15

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Lys His Glu Leu Tyr Val Ser Phe Arg Asp Leu Gly Trp Gln Asp Trp 35 40 45

Ile Ile Ala Pro Glu Gly Tyr Ala Ala Phe Tyr Cys Asp Gly Glu Cys
50 60

Ser Phe Pro Pro Asn Ala His Met Asn Ala Thr Asn His Ala Ile Val 65 70 75 80

Gln Thr Leu Val His Leu Met Phe Pro Asp His Val Pro Lys Pro Cys
85 90 95

Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp 100 105 110

Ser Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ser 115 120 125 WO 2005/085281 PCT/EP2005/002328

Cys Gly Cys His

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<211> 132

<212> PRT

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<223> BMP-6 mutein

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Ser Ser Ala Ser Asp Tyr Asn Ser Ser Glu Leu Lys Thr Ala Cys Arg 20 25 30

Lys His Glu Leu Tyr Val Ser Phe Gln Asp Leu Gly Trp Gln Asp Trp 35 40 45

Ile Ile Ala Pro Lys Gly Tyr Ala Ala Asn Tyr Cys Asp Gly Glu Cys 50 60

Ser Phe Pro Pro Asn Ala His Met Asn Ala Thr Asn His Ala Ile Val 65 70 75 80

Gln Thr Leu Val His Leu Met Asn Pro Glu Tyr Val Pro Lys Pro Cys 85 90 95

Cys Ala Pro Thr Lys Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp 100 105 110

Asn Ser Asn Val Ile Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala 115 120 125

Cys Gly Cys His

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<211> 139

<212> PRT

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Asn Gln Glu Ala Leu Arg Met Ala Asn Val Ala Glu Asn Ser Ser Ser 20 25 30

Asp Gln Arg Gln Ala Cys Lys Lys His Glu Leu Tyr Val Ser Phe Arg 35 40 45

Asp Leu Gly Trp Gln Asp Trp Ile Ile Ala Pro Glu Gly Tyr Ala Ala 50 55

Tyr Tyr Cys Glu Gly Glu Cys Ala Phe Pro Pro Asn Ser Tyr Met Asn 65 70 75 80

Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His Phe Ile Asn Pro 85 90 95

Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln Leu Asn Ala Ile 100 105 110

Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile Leu Lys Lys Tyr 115 120 125

Arg Asn Met Val Val Arg Ala Cys Gly Cys His

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<211> 139

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Pro Gln Ala Asn Arg Leu Pro Gly Ile Phe Asp Asp Val His Gly Ser 20 25 30

His Gly Arg Gln Val Cys Arg Arg His Glu Leu Tyr Val Ser Phe Gln

45

40

Asp Leu Gly Trp Leu Asp Trp Val Ile Ala Pro Gln Gly Tyr Ser Ala 50 60

Tyr Tyr Cys Glu Gly Glu Cys Ser Phe Pro Pro Asp Ser Cys Met Asn 70 75 80

Ala Thr Asn His Ala Ile Leu Gln Ser Leu Val His Leu Met Lys Pro 85 90 95

Asn Ala Val Pro Lys Ala Cys Cys Ala Pro Thr Lys Leu Ser Ala Thr 100 105 110

Ser Val Leu Tyr Tyr Asp Ser Ser Asn Asn Val Ile Leu Arg Lys His 115 120 125

Arg Asn Met Val Val Lys Ala Cys Gly Cys His 130

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<223> GDF-5 mutein

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1 10 15

Ala Arg Cys Ser Arg Lys Ala Leu His Val Asn Phe Lys Asp Met Gly 20 25 30

Trp Asp Asp Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Phe His Cys 35 40 45

Glu Gly Leu Cys Glu Phe Pro Pro Arg Ser His Leu Glu Pro Thr Asn 50 55 60

His Ala Val Ile Gln Thr Leu Met Asn Ser Met Asp Pro Glu Ser Thr 65 70 75 80

Pro Pro Thr Cys Cys Val Pro Thr Arg Leu Ser Pro Ile Ser Ile Leu 85 90 95

Phe Ile Asp Ser Ala Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met 100 105 110

Val Val Glu Ser Cys Gly Cys Arg 115 120

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<222> (1)..(120)

<223> GDF-6 mutein

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Thr Ala Phe Ala Ser Arg His Gly Lys Arg His Gly Lys Lys Ser Arg
1 10 15

Leu Arg Cys Ser Arg Lys Pro Leu His Val Asn Phe Lys Glu Leu Gly 20 25 30

Trp Asp Asp Trp Ile Ile Ala Pro Leu Glu Tyr Glu Ala Tyr His Cys 35 40 45

Glu Gly Val Cys Asp Phe Pro Pro Arg Ser His Leu Glu Pro Thr Asn 50 55 60

His Ala Ile Ile Gln Thr Leu Met Asn Ser Met Asp Pro Gly Ser Thr 65 70 75 80

Pro Pro Ser Cys Cys Val Pro Thr Lys Leu Thr Pro Ile Ser Ile Leu 90 95

Tyr Ile Asp Ala Gly Asn Asn Val Val Tyr Lys Gln Tyr Glu Asp Met 100 105 110

Val Val Glu Ser Cys Gly Cys Arg 115 120

<210> 31

<211> 146

<212> PRT

<213> Mus musculus

<220>

<221> MISC FEATURE

<222> (1)..(146)

<223> GDF-7 mutein

<400> 31

Thr Ala Leu Ala Gly Thr Arg Gly Ala Gln Gly Ser Gly Gly Gly 1 5 10 15

Ala Gly Arg Gly His Gly Arg Arg Gly Arg Ser Arg Cys Ser Arg Lys
35
40
45

Ser Leu His Val Asp Phe Lys Glu Leu Gly Trp Asp Asp Trp Ile Ile 50 55

Ala Pro Leu Asp Tyr Glu Ala Tyr His Cys Glu Gly Val Cys Asp Phe 70 75 80

Pro Pro Arg Ser His Leu Glu Pro Thr Asn His Ala Ile Ile Gln Thr 85 90 95

Leu Leu Asn Ser Met Ala Pro Asp Ala Ala Pro Ala Ser Cys Cys Val 100 105 110

Pro Ala Arg Leu Ser Pro Ile Ser Ile Leu Tyr Ile Asp Ala Asn 115 120 125

Asn Val Val Tyr Lys Gln Tyr Glu Asp Met Val Val Glu Ala Cys Gly 130 140

Cys Arg 145

<210> 32

<211> 108

<212> PRT

<213> Homo sapiens

<220>

<221> MISC\_FEATURE

<222> (1)..(108)

<223> BMP-10 mutein

<400> 32

Asn Ala Lys Gly Asn Tyr Cys Lys Arg Thr Pro Leu Tyr Ile Asp Phe 1 5 10

Lys Glu Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Pro Gly Tyr Glu 20 25 30 Ala Tyr Glu Cys Arg Gly Val Cys Asn Tyr Pro Pro Ala Glu His Leu 35 40 45

Thr Pro Thr Lys His Ala Ile Ile Gln Ala Leu Val His Leu Lys Asn 50 55

Ser Gln Lys Ala Ser Lys Ala Cys Cys Val Pro Thr Lys Leu Glu Pro 65 70 75 80

Ile Ser Ile Leu Tyr Leu Asp Lys Gly Val Val Thr Tyr Lys Phe Lys
85 90 95

Tyr Glu Gly Met Ala Val Ser Glu Cys Gly Cys Arg 100 105

<210> 33

<211> 110

<212> PRT

<213> Homo sapiens

<220>

<221> MISC FEATURE

<222> (1)..(110)

<223> GDF-2 mutein

<400> 33

Ser Ala Gly Ala Gly Ser His Cys Gln Lys Thr Ser Leu Arg Val Asn 1 5 10 15

Phe Glu Asp Ile Gly Trp Asp Ser Trp Ile Ile Ala Pro Lys Glu Tyr 20 25 30

Glu Ala Tyr Glu Cys Lys Gly Gly Cys Phe Phe Pro Pro Ala Asp Asp 35 40 45

Val Thr Pro Thr Lys His Ala Ile Val Gln Thr Leu Val His Leu Lys 50 . 55 60

Phe Pro Thr Lys Val Gly Lys Ala Cys Cys Val Pro Thr Lys Leu Ser 70 75 80

Pro Ile Ser Val Leu Tyr Lys Asp Asp Met Gly Val Pro Thr Leu Lys
85 90 95

Tyr His Tyr Glu Gly Met Ser Val Ala Glu Cys Gly Cys Arg
100 105 110